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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/921,406	08/02/2001	Zohar Yakhini	10010313-1 (2003309-0012)	6019

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EXAMINER

NICKOL, GARY B

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 12/12/2003

18

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/921,406	YAKHINI ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 23 July 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-4 and 21-24 is/are pending in the application.
- 4a) Of the above claim(s) 21-24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
     a) ☐ All    b) ☐ Some \*    c) ☐ None of:  
         1. ☐ Certified copies of the priority documents have been received.  
         2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
         3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
     a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                   | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                          | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>13</u> . | 6) <input type="checkbox"/> Other: _____                                    |

### **DETAILED ACTION**

The Election filed July 23, 2003 (Paper No. 16) in response to the Office Action of May 20, 2003 is acknowledged and has been entered.

Claims 21-24 were newly added and have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions.

Claims 5-20 were cancelled.

Claims 1-4 are pending and are currently under consideration.

Applicant's election with traverse of Group I, claims 1-4 in Paper No. 16 is acknowledged. The traversal is on the ground(s) that the claimed invention of diagnosing an aggressive form of cancer is based on determining the expression of a collection of genes chosen from the genes recited in claim 1. Applicant submits that part of the inventors' contribution to the art was identifying "the set of genes" listed in claim 1, as important in diagnosing aggressive forms of cancer. Thus, applicants submit the breadth of patent protection necessary for adequate coverage of the inventors' contribution to the art "must include a claim including all twenty genes". Applicants further argue that searching multiple genes does not place a serious burden on the examiner. These arguments have been carefully considered but are not found persuasive. The specification (page 2, line 15) clearly sets forth that the invention for diagnosing aggressive forms of cancer includes analyzing the expression "for one or more" of the genes listed in Claim 1. Thus, the claimed invention does not necessitate a search and examination of all twenty genes.

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Further, a search and examination of all twenty genes would impose a serious burden on the examiner because each gene comprises distinctly different structural and functional qualities, all of which would necessitate numerous searches throughout a multitude of different databases. And, although the inventions are similarly classified, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not coextensive and is much more important in evaluating the burden of search. Different searches and issues are involved in the examination of each group. Finally, restrictions can be required in applications where the generic claims recite such a multiplicity of species that an unduly extensive and burdensome search is necessary. MPEP 809.02(d). For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

### *Specification*

The specification is objected to because it contains embedded hyperlinks and/or other forms of browser-executable codes (i.e., see page 6, line 9; page 31, line 21 & 23). See MPEP §608.01. Patent publications of website addresses are permitted, but direct linkage to said sites must be disabled since USPTO policy does not permit the USPTO to link to any commercial sites since the USPTO exercises no control over the organization, views or accuracy of the information contained on these outside sites.

The specification is further objected to on pages 14-17, because there is no sequence identifier (e.g. SEQ ID NO.) to identify the Wnt5a mRNA. Applicant should amend the specification by inserting the appropriate SEQ ID NO.

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The specification is further objected to on page 51, line 14 for reciting, "figure 6 shows the top 22 genes" as it does not appear that figure 6 shows 22 genes.

### ***Drawings***

Color photographs and color drawings are acceptable only for examination purposes unless a petition filed under 37 CFR 1.84(a)(2) is granted permitting their use as acceptable drawings. In the event that applicant wishes to use the drawings currently on file as acceptable drawings, a petition must be filed for acceptance of the color photographs or color drawings as acceptable drawings. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and, unless already present, an amendment to include the following language as the first paragraph of the brief description of the drawings section of the specification:

The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings have been satisfied.

### ***Claim Objections***

Claim 1 is objected to because it includes nonelected subject matter. The objection can be obviated by amending the claim to only include the elected subject matter, Wnt5a.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite “identifying the tumor as aggressive or non-aggressive based on the expression pattern of the genes”; however it is not clear *how* the expression pattern provides a nexus for determining whether or not the tumor is aggressive or nonaggressive. The specification teaches (page 51) that melanoma samples with high levels of Wnt5a expression were more aggressive tumors than those with lower levels. Thus, it appears that the claims lack an essential or critical step.

Claims 1-3 are further rejected for reciting, “analyzing a set of genes” in conjunction with the Markush grouping of alternative genes. A set of genes is inherently more than one, yet the claims also include the wording “selected from the group consisting of” which means that only one gene may meet the limitations. Hence, the claims appear to lack a clear antecedent basis for the steps of the method.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, and 3-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Iozzo *et al.* (Cancer Research, Vol. 55, pages 3495-3499, 1995).

Iozzo *et al.* teach a method of diagnosing a form of cancer comprising providing a genetic sample from a test sample of a tumor and analyzing expression of the Wnt5a gene wherein the cancer is a malignant melanoma. Specifically, Iozzo *et al.* identify (page 3498, 2<sup>nd</sup> column; page 3499, last paragraph) statistically high levels of Wnt5a expression in lung carcinomas, metastatic melanomas, and breast carcinomas. Hence, based on the high pattern of expression of Wnt5a in these tumors, the authors have identified tumors that *inherently* possess the aggressive or non-aggressive phenotype.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Iozzo *et al.* (Cancer Research, Vol. 55, pages 3495-3499, 1995).

Iozzo *et al.* teach as set forth above.

Iozzo *et al.* do not specifically teach selecting a treatment regimen for an individual with the tumor based on whether the tumor is aggressive or non-aggressive.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to include the step of selecting a treatment regimen (such as chemotherapy or surgical removal of the tumor) for an individual who has been diagnosed with any one of the aggressive or non-aggressive tumors diagnosed by Iozzo *et al.* One would have been motivated to do so because the diagnosis of an aggressive or non-aggressive form of cancer usually requires that the clinician present the patient with some type of treatment option to lower the risk of mortality.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 703-305-7143. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the



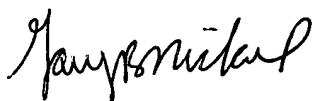
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organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary B. Nickol, Ph.D.  
Examiner  
Art Unit 1642

GBN  
December 11, 2003

A handwritten signature in cursive script, appearing to read "Gary B. Nickol", is written in dark ink.